Maintaining Healthy Glucose Control

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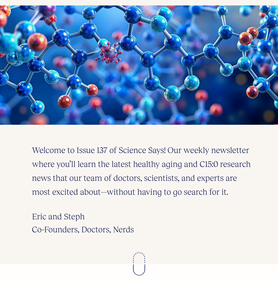

Welcome to Issue 137 of Science Says! Our weekly newsletter where you'll learn the latest healthy aging and C15:0 research news that our team of doctors, scientists, and experts are most excited about—without having to go search for it.

Eric and Steph
Co-Founders, Doctors, Nerds

What Dr. Stephanie Venn-Watson, our co-founder and author of *The Longevity Nutrient* and over 80 peer-reviewed scientific publications, is reading.

HEALTHY AGING

The C15:0 Science Behind Glucose, Insulin & Liver Health

The American Heart Association had a conference in New Orleans a few months ago, and they recently published scientific abstracts from this meeting in their journal, called Circulation. Among the many research reports was a longitudinal study that evaluated links between specific dietary fatty acids, including C15:0, and key markers of glucose, insulin and liver health. Let's dive into what this study found.

But first, how are glucose and liver health related?

Good question. The liver is a major determinant of our glucose control. Here's why:

- Our liver makes glucose and releases it into the bloodstream- ideally, when our glucose levels are low.
- The liver also stores glucose when levels are high, even more so than muscle and fat tissue.

As such, a healthy functioning liver helps us maintain healthy glucose levels.

Got it. Where does insulin come into the picture?

Insulin is an important cog that keeps our metabolism healthy.

- Insulin, made by islet beta cells in our pancreas, is a hormone that helps to shuttle glucose into cells - including our liver cells- to help keep our circulating glucose levels even-steven.
- Resistance to the body's response to insulin results in both imbalanced glucose and liver function.
- As a plot twist, and as described in part by Deng et al., abnormal iron metabolism and ferroptosis driven by the liver can spill over to the pancreas, resulting in imbalanced insulin.

Now that you know that, let's get to the study from the recent AHA conference.

What did the recent study evaluate?

In their study, Yehia et al. followed 460 people for 9 years to evaluate longitudinal associations between four dairy-based fatty acids (specifically, C15:0, t16:1n9, t18:1n11, and conjugated linoleic acid) and:

- Insulin sensitivity
- Pancreatic beta cell function
- Alanine aminotransferase (high ALT is a biomarker of compromised liver function)

This team from the University of Toronto used sophisticated statistical models to best determine how or if these different fatty acids may influence glucose, insulin and liver health over time.

I'm leaning in. What did they find?

Of all four dairy-based fatty acids assessed, and after controlling for what is called a False Discovery Rate (or FDR), only one had significant associations with insulin sensitivity, pancreatic beta cell function, and liver function. And they were all positive associations (aka linked to better insulin sensitivity, pancreatic function and liver function - as in, lower ALT). Bet you can guess which fatty acid.

Yep, C15:0.

This finding is remarkably consistent with other studies, where C15:0 was the top fatty acid linked to better health in longitudinal studies. This is because C15:0 has proven activities that directly support long-term health, including supporting insulin, glucose, and liver health.

Beyond association, how does C15:0 support insulin, glucose, and liver health?

In their impressive series of studies, Fu et al. demonstrated that pure C15:0:

- Activates AMPK, which is a well-known mechanism to support glucose control.
- Improves glucose uptake by muscle cells.
- Improves insulin sensitivity in cells.
- Enabled glucose uptake that was as good as insulin (aka, C15:0 actually served as an insulin mimic).

Yes, that last one was a surprising finding. What is becoming less surprising is the consistent role of C15:0 as a metabolic balancer. Consistent with the cell-based and prospective human studies above, C15:0 effectively lowered glucose in a relevant animal model within 12 weeks.

Regarding the liver,

- Bishop et al. showed that C15:0 activated AKT, which improves insulin sensitivity in liver cells.
- Our own studies demonstrated that C15:0 also activates PPARs, which are liver protective. We also showed that C15:0 lowers unwanted iron deposition in the liver.
- Further, Wei et al. showed that relevant animal models supplemented with pure C15:0 had healthier liver function (lower AST and ALT), lower proinflammatory cytokines, and lower lipid peroxidation in the liver.
- Meanwhile, a randomized placebo controlled clinical trial by Robinson et al. demonstrated that C15:0 supplementation raised C15:0 levels, and when people achieved levels greater than 5 ug/ml, they also had improved liver function (aka, lower AST and ALT) within 12 weeks. Which was well aligned with the recent Yehia et al. study.

Bottom line, robust science continues to support that C15:0 plays a key role in keeping our insulin, glucose and liver health in tip-top shape. Go, science.

Have a wonderful week, everyone!

Dive deeper into the science

READ THE RELEVANT STUDIES

- Yehia et al. Longitudinal associations of dairy derived serum fatty acids: findings from the prospective metabolism and islet cell evaluation (PROMISE) cohort
- Sherwin, R. Role of liver in glucose homeostasis
- Bo et al. Insulin and liver health
- Deng et al. Iron metabolism, ferroptosis and islet beta cells
- Santaren et al. Serum C15:0 is associated with better metabolic health and beta-cell function
- Fu et al. Pentadecanoic acid promotes basal and insulin-stimulated glucose uptake in C2C12 myotubes
- Venn-Watson et al. Efficacy of dietary odd-chain saturated fatty acid pentadecanoic acid parallels broad associated health benefits in humans: could it be essential?
- Bishop et al. C15:0 activates AKT and lowers proinflammatory cytokines in liver cells
- Wei et al. Parabacteroides distasonis uses dietary inulin to support liver health via pentadecanoic acid
- Robinson et al. C15:0 Supplementation in Young Adults at Risk for Metabolic Syndrome: A Randomized Controlled Trial

- Nerd out on all the C15:0 science at DiscoverC15.com